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TRANSMITTAL FORM

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First Named Inventor	Juan Luis HANCKE
Group Art Unit	1625
Examiner Name	N. RAHMANI, Esq.
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ENCLOSURES *(check all that apply)*

- ☒ Fee Transmittal Form
  - ☒ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
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- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
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- ☐ Assignment Papers *(for an Application)*
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- ☐ Proprietary Information
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

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In The United States Patent Office

In re Application of Juan Luis HANCKE
et al., *Diterpenic Lambdanes...*

Art Unit 1625
Serial No. 10/516,500
Filed 3 Februry 2004

APPEAL BRIEF

11/08/2006 TL0111 00000084 10516500
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TABLE OF AUTHORITIES

CASES

OTHER AUTHORITIES

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INTRODUCTION

This APPEAL BRIEF is submitted pursuant to the earlier-submitted NOTICE OF APPEAL. Enclosed please find the large-entity fee for filing an appeal brief. This APPEAL BRIEF is filed within two months of the earlier-submitted NOTICE OF APPEAL. No extension of time fee is therefore believed due.

This patent application has been granted Special status. Expedited resolution of this appeal is therefore respectfully requested.

Real Party In Interest

The real party in interest is HP Ingredients, Inc., a Florida corporation.

Related Appeals and Interferences

There are no related appeals nor interferences known to appellant, the appellant's legal representative, nor the assignee which may be related to, directly affect nor be directly affected by or have a bearing on the Board's decision in the immediate appeal.

Status of Claims

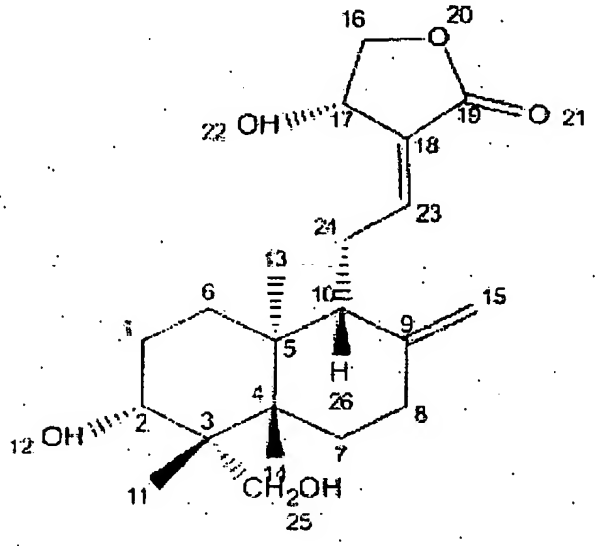
Claims 1 to 52 stand cancelled. Claims 53 to 73 are pending and stand twice rejected. Appellant appeals the rejection of all pending claims.

Status of Amendments

No amendment has been filed subsequent to the Final rejection.

Summary of Claimed Subject Matter

The invention relates to a compound (3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone) and its use to treat certain medical conditions.



The inventors believe that this compound is effective in modulating the activity of the human immune system, and will therefore be effective in treating conditions exhibiting an under-active or over-active immune response. Three independent claims are pending.

Independent claim 53 claims the use of 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl] ethylidene]-dihydro-4-hydroxy-2(3h)-furanone to treat autoimmune disease, Acquired Immune

Deficiency Syndrome or Alzheimer's Disease. *See e.g.,* SPECIFICATION at 13:1 *et seq.*; 2:23 *et seq.*; 6:9 *et seq.*[1]

Independent claim 66 claims the use of 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone to modulate a patient's immune system function (e.g., to activate peroxysome proliferator activated receptor γ. *E.g., id.* at 6:9 *et seq.*

Independent claim 73 claims the use of 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone to treat "syndrome X," a condition which the inventors believe is caused by immune system dysfunction. *E.g., id.* at claim 73.

Grounds of Rejection to be Reviewed on Appeal

The grounds for rejection presented on appeal are as follows:

Whether the OFFICE ACTION states a *prima facie* case that claim 73 is not enabled?

Whether the OFFICE ACTION states a *prima facie* case that claims 53 to 73 fail to comply with Section 112, first paragraph?

Whether the OFFICE ACTION states a *prima facie* case that claims 53 to 73 are anticipated under Section 102(b)?

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[1] To avoid confusion, all references to the Specification are to the clean (not the black lined) version of the SUBSTITUTE SPECIFICATION received by the Office on 02 December 2004.

Argument

Applicant respectfully believes the Examiner has failed to provide a sustainable rationale to reject any claim. The claims argued separately are placed under sub-headings including the relevant claim number. Applicant here quotes the 16 March 2006 OFFICE ACTION rather than the 31 August 2006 FINAL OFFICE ACTION, when the FINAL ACTION simply states that the rejections are maintained "for the reasons of record."

THE OFFICE ACTION FAILS TO STATE A *PRIMA FACIE* CASE OF FAILURE TO PROVIDE AN ENABLING DISCLOSURE

The Examiner fails to state a prima facie case that claim 73 is not enabled

Claim 73 covers a method comprising: i) identifying in a person the possible presence of Syndrome X, and ii) administering to said person: *Andrographis paniculata*; or an *Andrographis paniculata* extract containing 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone.

The Examiner rejects claim 73 for non-enablement. The Examiner argues, "Andrographis paniculata grown just anywhere everywhere on this planet may or my not have the compounds necessary to treat Syndrome X. Does this

extract of this plant, grown under any and all conditions, treat Syndrome X?" *See* OFFICE ACTION (31 August 2006) at 2.

Applicant respectfully asks the Board to reverse this rejection because the Examiner fails to state a *prima facie* case of non-enablement, nor provide any evidence to support her rejection.

The Examiner Fails To Plead A Prima Facie *Case That The Disclosure Fails to Enable the Claim*

The Applicants' Disclosure is Presumed to Be Enabling

Applicant's disclosure is presumed as a matter of law to be operative and enabling. *See In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). Furthermore, as long as the disclosure provides at least one method of making the claimed product, then the enablement requirement is satisfied. *In re Fischer*, 427 F.2d 833, 839 (C.C.P.A. 1970).

In the immediate case, the Specification provides at, *e.g.*, 17:15 to 25:29, "at least one method" of making the extract of claim 73. Thus, the Specification enables one to practice this claim as a matter of law. *See In re Fischer.*

The Examiner fails to provide any evidence showing the amount of experimentation required

Furthermore, a *prima facie* case of non-enablement requires the Examiner to introduce into the record evidence showing that the amount of experimentation required to make the claimed invention is "undue." *E.g., Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916); *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976). The Board cannot sustain a rejection where the Examiner has not bothered to provide evidentiary support for it. *See e.g., In re Eynde*, 480 F.2d 1364, 1370 (C.C.P.A., 1973); *In re Barr*, 444 F.2d 588 (C.C.P.A., 1971); *In re Ahert*, 424 F.2d 1088, 1091 (C.C.P.A., 1970).

In the immediate case, the OFFICE ACTION fails to provide any evidence at all showing the amount of experimentation required. To the contrary, the Examiner merely speculates that experimentation may be required – *yet might not be.* ("Andrographis paniculata grown just anywhere everywhere on this planet may or my not have the compounds necessary") Such speculation fails to replace evidence showing the amount of experimentation required.

Applicant Provides Evidence That the Claim Is Enabled

Furthermore, one of the Inventors of record specifically contradicts the Examiner's baseless speculation, testifying:

> I have no reason to believe that "*Andrographis paniculata* ... may or my [*sic*] not have the compounds necessary to treat Syndrome X." To the contrary, **every** specimen of *Andrographis paniculata* which I have evaluated, **from whatever source or ecosystem**, has in fact contained "the compounds necessary to treat Syndrome X." I therefore know of no factual evidence to support the thesis that *Andrographis paniculata* from a certain specific ecosystem "may or my [*sic*] not have the compounds necessary to treat Syndrome X."

See J. L. HANCKE, RULE 132 DECLARATION (9 September 2006) at ¶ 4 (emphasis mine). The Board cannot rely on the Examiner's speculation because it is *baseless* and is specifically *contradicted* by the Inventor.

THE EXAMINER FAILS TO STATE A PRIMA FACIE CASE THAT CLAIMS 53 TO 73 VIOLATE THE WRITTEN DESCRIPTION REQUIREMENT

Claims 53 to 73 stand rejected under 35 U.S.C. 112, first paragraph "for reason of record." *See* OFFICE ACTION at 2, ¶ 4 (31 August 2006). The reason of record is an alleged failure to comply with the "written description" requirement. *See* OFFICE ACTION at 4, ¶ 7 (16 March 2006). Applicant respectfully asks the Board to reverse the Examiner because she has not bothered to provide you with the evidence needed to sustain her rejection.

The Original Disclosure Is Presumed To Provide An Adequate Written Description

The Inventors provide several actual reductions to practice

The description may fulfill the written description requirement in a number of ways. For example, if the disclosure contains an actual reduction to practice, then the disclosure fulfills the written description requirement. *See Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566 (Fed. Cir., 1997), *certiorari denied*, 523 U.S. 1089 (1998). (possession may be shown by describing an actual reduction to practice"). Thus, the Patent Office's own Guidelines say that where the disclosure contains an actual reduction to practice, this fulfills the requirement, and the Examiner should stop the analysis there. *See* United States Patent & Trademark Office, *Revised Interim Written Description Guidelines Training Materials* at page 7.

In the immediate case, the Examiner does not dispute that the disclosure at *e.g.*, pages 23 to 34, teaches actual reductions to practice. Thus, the original disclosure provides an adequate written description. *See Eli Lilly.*

The Inventors provide the precise chemical formula at issue

Alternatively, chemical formulae provide adequate written description. *See Eli Lilly* at 1568 ("In cases involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass").

In the immediate case, the Examiner does not dispute that the disclosure clearly teaches the specific formula for the claimed compound.

The Examiner Fails To Rebut This Presumption

A written description as filed is presumed adequate. *See In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). Given the presumption of adequacy, the burden is on the Examiner to provide a *reasonable factual basis* to challenge the adequacy of the written description. *See* MANUAL OF PATENT EXAM. PROC. § 2163.04. Thus, the Examiner "has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." *Id.*

*The Examiner fails to provide a reasonable **factual** basis for the rejection*

In the immediate case, the Examiner fails to provide a *reasonable factual basis* to challenge the adequacy of the written description. To the contrary,

the Examiner provides *no factual basis at all* to support its allegation that the claims contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) ... had possession of the claimed invention." Rather, the Examiner argues that the disclosure fails to provide a written description of something *different from* the claimed invention.

For example, the Examiner argues that "the specification does not enable the instant compound to alter the gene expression." *See* OFFICE ACTION (16 March 2006) at 6, 11, 14, 18, 22. "Altering gene expression," however, is not at issue here; to the contrary, the claims do not even mention "altering gene expression."

Similarly, the Examiner argues that "Applicant has not provided written description on how to diagnose a patient with any and all possible diseases known." *See* OFFICE ACTION (16 March 2006) at 5; *id.* at 6 ("the specification does not enable the instant compound to ... treat any and all known or unknown diseases"). This argument, however, is inapposite, because the claims at issue do not cover "any and all known or unknown diseases"; to the contrary, the claims enumerate specific

diseases (AIDS, Syndrome X, et cetera) known as, or suspected to be, disorders affecting the immune system.[2]

THE EXAMINER FAILS TO STATE A *PRIMA FACIE* CASE OF ANTICIPATION OF CLAIMS 53 TO 73

Claims 53 to 73 stand rejected as anticipated over John G. BABISH *et al.*, WO/96/17605 (1996); John G. BABISH *et al.*, U.S. Patent Publication No. 2002/0068098 (2002); Srinivas NANDURI *et al.*, U.S. Patent Publication No. 2002/0016324 (2002); Srinivas NANDURI *et al.*, U.S. Patent No. 6,410,590 (2002); Srinivas NANDURI *et al.*, U.S. Patent No. 6,486,196 (2002); Geoffrey D. WHEELOCK *et al.*, U.S. Patent No. 5,833,994 (1998); and Geoffrey D. WHEELOCK *et al.*, WO 98/30213 (1998).

Reconsideration is requested because the rather voluminous art of record fails to teach the claimed compound.

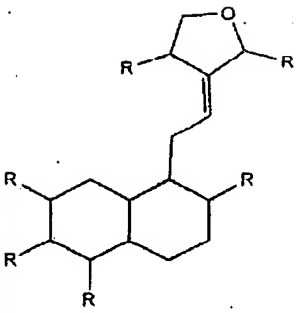
The Examiner fails to compare the prior art to the claims

The Examiner argues that "Andrographolide is well known in the art." The claims, however, do not require "andrographolide." Rather, the claims cover 3-

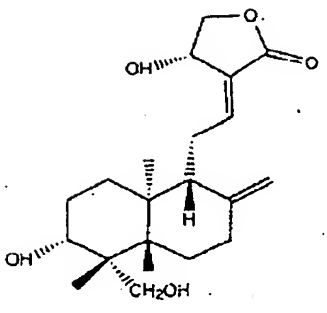
[2] Furthermore, the Examiner concedes that the art teaches diagnostic methods for each of the specific diseases at issue here. *See* OFFICE ACTION (16 March 2006) at 8, 20 ("autoimmune diseases, ... AIDS, etc. can be diagnosed by methods comprising determining from a sample ... an abnormally decreased or increased level of TR6 polypeptide or TR6 mRNA."). Because diagnostic methods are known in the art, Applicant need not provide an enabling disclosure of them.

[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidenc]-dihydro-4-hydroxy-2(3h)-furanone. This distinction is important because there is some confusion in the art regarding the meaning of the term "andrographolide." *See* J.L. HANCKE, RULE 132 DECLARATION (9 September 2006) at ¶ 6. Pointedly, the Examiner herself acknowledges that her own references confirm this. *See* OFFICE ACTION at 4 ("It is noted that Babish et al., 2002/0077350, and US 2002/0068098 have incorrect structure for Andrographolide.")

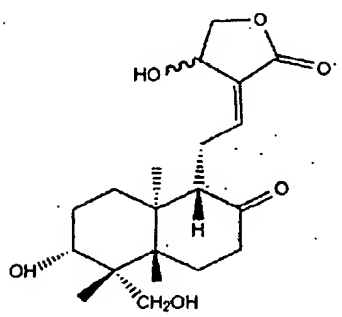
The claimed compound, 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone, is not taught by any reference of record. This is illustrated in the accompanying Figure:



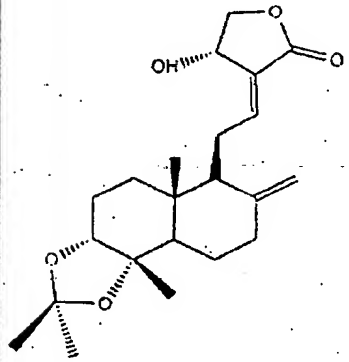
John G. BABISH *et al.*, WO '605



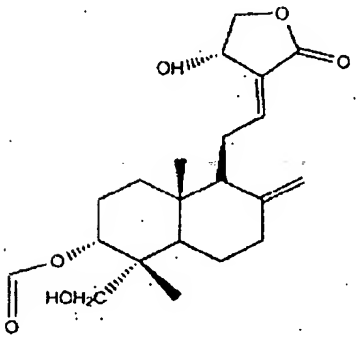
The claimed compound



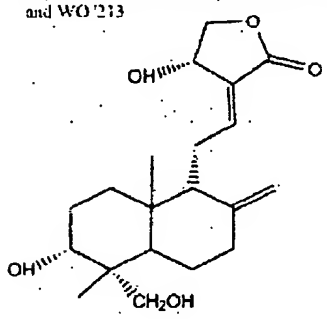
John G. BABISH *et al.*, U.S. '098
G.D. WHEELOCK *et al.*, U.S. '994; U.S. '063 and WO '213



NANDURI *et al.*, U.S. '324



NANDURI *et al.*, U.S. '196



NANDURI *et al.*, U.S. '590

For example, BABISH *et al.*, WO '605 and NANDURI *et al.*, U.S. '324, U.S. '590, and U.S. '196 (2002) fail to teach methylation at C4. Similarly, BABISH *et al.* U.S. '098, and WHEELOCK *et al.*, U.S. '994, U.S. '063 and WO '213 fail to teach oxidation at C9. No art of record teaches the claimed compound. *See* J.L. HANCKE, RULE 132 DECLARATION (9 September 2006) at ¶¶ 7-9; J.L. HANCKE, SUPPLEMENTAL RULE 132 DECLARATION (20 September 2006) at ¶¶ 1-4.

Further, the Examiner concedes that the predictability in the pharmaceutical art is low, because minor structural differences can precipitate major

changes in toxicology or clinical efficacy. This shows that it would not have been obvious to modify any of the prior art compounds to *make* the claimed compound, and that it would not have been obvious to *use* such a modified compound for the claimed uses.

Similarly, the claims are drawn to methods to treat AIDS, Syndrome X, non-autoimmune Alzheimer's Disease, and autoimmune disease. In contrast, the art of record fails to teach these therapeutic uses. *See* J.L. HANCKE, RULE 132 DECLARATION (9 September 2006) at ¶¶ 7-9.

NO PENDING REJECTION IS SUSTAINABLE

The claims are in condition for allowance. The Examiner has not bothered to try to provide the Board with the evidence the Board would need to sustain the Examiner's rejections.

Applicant therefore respectfully requests the Board reverse all pending rejections and order the Examiner to issue a NOTICE OF ALLOWANCE.

Respectfully submitted on behalf of the Applicant by its attorneys,
PHARMACEUTICAL PATENT ATTORNEYS, LLC

/s/
Mark Pohl, Reg. No. 35,325

Pharmaceutical Patent Attorneys LLC
55 Madison Avenue, 4th floor
Morristown, NJ 07960-6397 USA
8 November 2006

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CLAIMS APPENDIX

53. A method comprising:

i) diagnosing in a patient a disease selected from the group consisting of: Alzheimer's Disease; Acquired Immune Deficiency Syndrome; and autoimmune disease, and

ii) administering to said patent 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone in an amount effective to combat said disease.

54. The method of claim 53, wherein said disease comprises autoimmune disease.

55. The method of claim 54, wherein said autoimmune disease comprises rheumatoid arthritis.

56. The method of claim 54, wherein said autoimmune disease comprises lupus exanthematous.

57. The method of claim 54, wherein said autoimmune disease comprises multiple sclerosis.

58. The method of claim 54, wherein said autoimmune disease comprises asthma.

59. The method of claim 54, wherein said autoimmune disease comprises allergic reaction.

60. The method of claim 54, wherein said autoimmune disease comprises a condition selected from: systemic dermatomyocytis; and psoriasis.

61. The method of claim 54, wherein said autoimmune disease comprises osteoarthritis.

62. The method of claim 54, wherein said autoimmune disease comprises diabetes mellitus.

63. The method of claim 54, wherein said an amount effective to combat said disease comprises from about 1 mg to about 5 mg of 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone per day, per kilogram of patient body weight.

64. The method of claim 53, wherein said disease comprises Alzheimer's Disease.

65. The method of claim 53, wherein said disease comprises Acquired Immune Deficiency Syndrome.

66. A method comprising:

i) diagnosing in a patient a disease, and

ii) administering to said patent 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone in an amount effective to affect said patient's immune system function.

67. The method of claim 66, wherein said amount effective comprises an amount effective to activate peroxysome proliferator activated receptor γ.

68. The method of claim 66, wherein said amount effective comprises an amount effective to reduce the activity of an inflammatory cytokine.

69. The method of claim 68, said inflammatory cytokine comprising interleukin-2.

70. The method of claim 68, said inflammatory cytokine comprising interferon γ.

71. The method of claim 66, wherein said amount effective comprises an amount effective to inhibit NFκB.

72. The method of claim 66, wherein said amount effective comprises an amount effective to inhibit T-cell proliferation.

73. A method comprising:

i) identifying in a person the possible presence of Syndrome X, and

ii) administering to said person a substance selected from the group consisting of: *Andrographis paniculata*; and an *Andrographis paniculata* extract containing 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone; said substance administered in an amount effective to combat Syndrome X.

EVIDENCE APPENDIX

The two Rule 132 Declarations previously submitted in this case, and all other evidence relied on, has been submitted before filing of the NOTICE OF APPEAL. Physical copies of this evidence is not included here because the Board has access to this evidence via the PAIR system.

RELATED APPEALS APPENDIX

None.